

## AMENDMENT

(Amendment under Article 11)

To Examiner of the Patent Office

## 1. Identification of International Application

PCT/JP03/03944

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#### 4. Subject of Amendment

##### Specification and Claims

#### 5. Contents of Amendment

(1) "... both a mature fruit and an immature fruit, or an immature fruit of ..." described on page 5, lines 15 - 16 of the specification submitted on October 28, 2003 is amended to "... both a mature fruit and an immature fruit of ...".

(2) "... both a mature fruit and an immature fruit, or an immature fruit of ..." described on the page 6, lines 12 - 13, lines 18 - 19, line 25 - 26 of the same specification is amended to "... both a mature fruit and an immature fruit of ...".

(3) "... both the mature fruit and the immature fruit, or the immature fruit of ..." described on the page 7, lines 10 - 11 and line 25 of the same specification is amended to "... both the mature fruit and the immature fruit of ...".

(4) "... both a mature fruit and an immature fruit, or immature fruit of ..." described on the page 8, line 11 - 12 of the same specification is amended to "... both a mature fruit and an immature fruit of ...".

(5) "... both a mature fruit and an immature fruit, or an immature fruit of ..." described on the page 31, lines 3 - 4 of the same specification is amended to "... both a mature fruit and an immature fruit of ...".

(6) "... both a mature fruit and an immature fruit, or an immature fruit of ..." described in claim 1 on page 34 is amended to "... both a mature fruit and an immature fruit of ...".

(7) "... both the mature fruit and the immature fruit or the immature fruit of ..." described in claim 2 on page 34 is amended to "... both the mature fruit and the immature fruit of ...".

(8) "... both the mature fruit and the immature fruit or the immature fruit of ..." described in claim 3 on page 34 is amended to "... both the mature fruit and the immature fruit of ...".

(9) "... both the mature fruit and the immature fruit or the immature fruit of ..." described in claim 4 on page 34 is amended to "... both the mature fruit and the immature fruit of ...".

(10) "... both a mature fruit and an immature fruit or an immature fruit of ..." described in claim 6 on page 35 is amended to "... both a mature fruit and an immature fruit of ...".

#### 6. List of Attached Documents

(1) Specification: pages 5 - 8, page 31

(2) Claims: pages 34-35

further the side effects from the anticancer agents including death are becoming socially important problems.

On the other hand, humans and animals have inherent immune system which protects the body from pathogenic  
5 microorganisms. Since cancer cells are self-derived foreign substances generated in the body, in the case where the immunity is high, the cancer cells are typically removed by natural killer cells, macrophages and the like.

However, if the immunity is lowered due to aging or  
10 accumulated stress, cancer cells tend to proliferate.

An object of the invention described in claims 1 to 3 and 6 in the present inventions is to enhance the innate immune system such as natural killer cells, macrophages and the like, or the activity of lymphocytes, and thus obtain a  
15 higher immunopotentiating effect by using both a mature fruit and an immature fruit of a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), or a fruit of the genus *Pyrus*.

An object of the invention described in claim 4 is to  
20 enable suitable administration depending on the situation, in addition to the object of the invention described in claims 1 to 3.

## Disclosure of Invention

The present inventors have found that a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple  
5 (*Malus pumila*), a fruit of the genus *Pyrus*, or a substance derived therefrom, has the higher immunopotentiating effect by initially carrying out various animal tests, and then on humans, to thus complete the present inventions.

To achieve the above-mentioned objects, the invention  
10 described in claim 1 in the present inventions is directed to a drug such as an immunopotentiator, which is characterized by comprising both a mature fruit and an immature fruit of a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), a fruit of  
15 the genus *Pyrus*, or a substance derived therefrom as an active ingredient.

The invention described in claim 2 is characterized by the constitution of using an aqueous extract of both mature fruit and an immature fruit of the fruit of the genus *Malus*  
20 such as apple (*Malus domestica*) and crabapple (*Malus pumila*), the fruit of the genus *Pyrus*, or a substance derived from the aqueous extract, in addition to the constitution of the invention described in claim 1.

The invention described in claim 3 is characterized by  
25 the constitution of using an extract both mature fruit and

an immature fruit of the fruit of the genus *Malus* such as  
apple (*Malus domestica*) and crabapple

(*Malus pumila*), the fruit of the genus *Pyrus* obtained by extraction with an organic solvent such as alcohol, or a substance derived from the extract, in addition to the constitution of the invention described in claim 1.

5       The organic solvent such as alcohol herein includes, for example, acetone, ether, ethyl acetate, chloroform, and methylene chloride.

It has been revealed that the effects of invention described in claims 1 to 3 obtained from such constitutions,  
10   consist in that both the mature fruit and the immature fruit of a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), a fruit of the genus *Pyrus*, a substance therefrom, an extract obtained by extracting the fruit with water or an organic solvent such  
15   as alcohol, or a substance derived from the extract, when administered, enhances the immune system such as natural killer cells, macrophages and the like to control cancer-attacked cells, as well as to prevent carcinogenesis of cells not yet attacked by cancer, and when taken regularly,  
20   obtain higher immunopotentiating effect and thus has the effect of preventing the onset of cancer, that is, the cancer preventing effect.

The invention described in claim 4 is characterized by the constitution of administering as a raw material an  
25   extract of both the mature fruit and the immature fruit of

the fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), the fruit of the genus *Pyrus*, or a substance derived from the extract orally,



percutaneously, parenterally, or via other routes, in addition to the constitution of the invention described in claim 1, 2 or 3.

5 The effect of invention described in claim 4 obtained from such constitution in addition to the effects of the invention described in claim 1, 2 or 3, consists in that it enables percutaneous administration, parenteral administration and administration via other routes, although oral administration is a general administration route.

10 The invention described in claim 6 is a health food for enhancing immune system, comprising the mature fruit and the immature fruit of a fruit of the genus Malus such as apple

As described above, it has been observed that the invention described in claims 1 to 3 or 6 in the present inventions has the effects that both a mature fruit and an immature fruit of a fruit of the genus *Malus* such as apple (Malus domestica) and crabapple (Malus pumila), a fruit of the genus *Pyrus*, a substance derived therefrom, an extract by extracting the fruit with water or an organic solvent such as alcohol, or a substance derived from the extract, when administered, enhances the innate immune system such as natural killer cells, macrophages and the like to control cancer-attacked cells, as well as to prevent carcinogenesis of cells not yet attacked by cancer, and when taken regularly, has the effect of preventing the onset of cancer, that is, the cancer preventing effect.

In other words, administration of a fruit of the genus *Malus* such as apple (Malus domestica) and crabapple (Malus pumila), a fruit of the genus *Pyrus*, or a substance derived therefrom could enhance the innate immune system such as natural killer cells, macrophages and the like, and the activity of lymphocytes, inhibit the onset or growth of cancer cells, and prevent or suppress cancer.

Further, it has been proven that it could suppress or control cancer more effectively, as compared to the extract of *Cordyceps sinensis* which has conventionally been suggested as an immunopotentiator.

Further, it has been found that by administering a